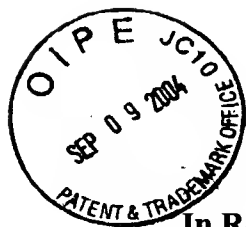


09-10-04

Jpw 1635

DOCKET NO.: ISIS-4804

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Muthiah Manoharan, et al.

Confirmation No.: 3997

Application No.: 09/996,292

Group Art Unit: 1635

Filing Date: November 28, 2001

Examiner: Janet L. Epps Ford

For: NUCLEASE RESISTANT CHIMERIC OLIGONUCLEOTIDES

EXPRESS MAIL LABEL NO: EL999288103US

DATE OF DEPOSIT: September 9, 2004

EL999288103US

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

- ☐ In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in § 1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or

before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

- ☒ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.116 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

☒ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of \$180.00 as set forth in § 1.17(p) is attached.

- ☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of \$180.00 as set forth in § 1.17(p).

- ☒ Copies of reference numbers 13-30 listed on the attached Form PTO-1449 are enclosed herewith.

- ☐ Copies of reference numbers - on the attached Form PTO 1449 are not required to be submitted pursuant to 37 CFR § 1.98(a)(2)(i).

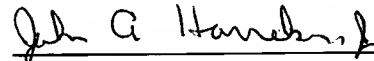
- ☐ Copies of references - are not being submitted because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application number , filed for which a claim for priority under 35 U.S.C. § 120 has been made in the instant application.

- ☐ The relevance of those listed references which are not in the English language is as follows:

There are no listed references which are not in the English language.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

Date: 9/9/04



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DOCKET NO.: ISIS-4804

PATENT



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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

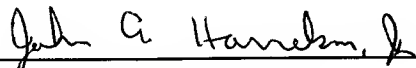
**CERTIFICATION UNDER 37 CFR § 1.97(e)**

In accordance with 37 CFR § 1.97(e), certification is hereby made that:

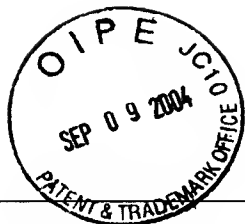
- ☒ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the Information Disclosure Statement.
- ☐ No item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after

making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

Date: 9/9/04

  
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<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office	Docket No. ISIS-4804	Application No. 09/996,292
	Applicant Muthiah Manoharan, et al.	
	Filing Date November 28, 2001	Group 1635
	Confirmation No. 3997	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
13	Copy of the PCT International Search Report dated August 20, 2004 (PCT/US02/20934)	
14	Barawkar, D.A., et al., "Synthesis, biophysical properties, and nuclease resistance properties of mixed backbone oligodeoxynucleotides containing cationic internucleoside guanidinium linkages: deoxynucleic guanidine/DNA chimeras," <i>Proc. Natl. Acad. Sci. USA</i> , <b>1998</b> , 99, 11047-11052	
15	Caulfield, T.J., et al., "Achiral internucleoside linkages: CH <sub>2</sub> -CH <sub>2</sub> -NH and NH-CH <sub>2</sub> -CH <sub>2</sub> linkages," <i>Bioorganic &amp; Medicinal Chem. Letts.</i> , <b>1993</b> , 3(12), 2771-2776	
16	Hirao, I., et al., "Most compact hairpin-turn structure exerted by a short DNA fragment, d(GCGAAGC) in solution: an extraordinarily stable structure resistance to nucleases and heat," <i>Nucleic Acids Res.</i> , <b>1994</b> , 22(4), 576-582	
17	Karpeisk, M., et al., "Substrate specificity of nuclease S <sub>1</sub> from <i>aspergillus oryzae</i> in hydrolysis of low molecular weight substrates," Institute of Molecular Biology, USSR, Moscow, <b>1982</b> , 8(3), 386-395 ( <b>English abstract on page 395</b> )	
18	Kuznetsova, M.A., et al., "Hybridization properties and nuclease resistance of oligo (2'-O-tetrahydropyranylrbonucleotides," <i>J. of Bioorganic Chem.</i> , <b>2000</b> , 26(1), 78-80	
19	Peyrottes, S., et al., "Synthesis, base pairing properties and nuclease resistance of oligothymidylate analogs containing methoxyphosphoramidate internucleoside linkages," <i>Nucleosides &amp; Nucleotides</i> , <b>1994</b> , 13(10), 2135-2149	
20	Quartin, R.S., et al., "Number and distribution of methylphosphonate linkages in oligodeoxynucleotides affect exo- and endonuclease sensitivity and ability to form RNase H substrates," <i>Nucleic Acids Res.</i> , <b>1989</b> , 17(18), 7253-7362	
21	Sun, J.S., et al., "Triple-helix formation by $\alpha$ oligodeoxynucleotides and $\alpha$ oligodeoxynucleotide-intercalator conjugates," <i>Proc. Natl. Acad. Sci. USA</i> , <b>1991</b> , 88, 6023-6027	
22	Zhao, Z., et al., "synthesis and preliminary biochemical studies with 5'-deoxy-5'-methylidene phosphonate linked thymidine oligonucleotides," <i>Tetrahedron Letts.</i> , <b>1996</b> , 37(35), 6239-6242	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>



<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office	Docket No. ISIS-4804		Application No. 09/996,292	
	Applicant Muthiah Manoharan, et al.			
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	Confirmation No. 3997			
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>				
	23	Yoshizawa, S., et al., "Nuclease resistance of an extraordinarily thermostable mini-hairpin DNA fragment, d(GCGAAGC) and its application to <i>in vitro</i> protein synthesis," <i>Nucleic Acids Res.</i> , <b>1994</b> , 22(12), 2217-2221		
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>		



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	Filing Date November 28, 2001	Group 1635
	Confirmation No. 3997	

**U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass

**FOREIGN PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	24	WO 92/02534 A2	02/20/92	PCT		
	25	WO 92/03464 A1	03/05/92	PCT		
	26	WO 95/25814 A1	09/28/95	PCT		
	27	WO 95/26972 A1	10/12/95	PCT		
	28	WO 99/24452 A2	05/20/99	PCT		
	29	WO 01/57188 A2	08/09/01	PCT		
	30	WO 03/004602 A2	01/16/03	PCT		

<b>EXAMINER</b>	<b>DATE CONSIDERED</b>
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